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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,689	03/25/2004	Mark Larche	3652/2004	7876

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PALMER & DODGE, LLP
KATHLEEN M. WILLIAMS
111 HUNTINGTON AVENUE
BOSTON, MA 02199

EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	
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11/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,689	LARCHE ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,13 and 16-29* is/are pending in the application.

4a) Of the above claim(s) *16-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/24/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-5, 13 and 16-29 are pending.

2. Claims and 16-29 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1-5 and 13 are currently under examination as they read on a method of desensitizing a patient to a polypeptide allergen comprising administering to the patient a peptide wherein restriction to DR4 possessed by the patient can be demonstrated for the peptide and the peptide is able to induce a late phase response in an individual who possesses DR4.

4. Applicant's IDS document submitted 04/24/2007 is acknowledged.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures mailed on 03/28/2007.

Applicant's arguments filed on 08/28/2007 have been fully considered, but are not found persuasive.

Applicants argue that they are preparing a corrected sequence listing and will file it with the PTO under separate cover.

It is the Examiner's position that no such sequence listing has been received by the PTO.

Specification

6. The specification stands objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence for the same reasons as set forth in the Office Action mailed on 03/28/2007.

Applicant's arguments filed on 08/28/2007 have been fully considered, but are not found persuasive.

Applicants argue that they are preparing a corrected sequence listing and will file it with the PTO under separate cover.

It is the Examiner's position that no such sequence listing has been received by the PTO.

7. In view of the amendment filed on 08/28/2007, only the following rejections are maintained.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5 and 13 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants are not enabled for a method of desensitising a patient to a **polypeptide allergen** the method comprising administering to the patient **a peptide derived from the allergen** wherein restriction to a MHC Class II molecule possessed by the patient can be demonstrated for the peptide and **the peptide** is able to induce a late phase response in an individual who possesses the said MHC Class II molecule, wherein the **peptide has a length of 5 to 50 amino acids** and is not a Fel d I-derived peptide of claim 1; wherein **the peptide** is included in a composition containing **a plurality of peptides derived** from the **said allergen** of claim 2; wherein the **plurality of peptides derived** from said allergen includes **peptides** for which restriction to Class II DR molecules DR2, DR3, DR4 and DR7 can be demonstrated, provided that such **peptides** can be derived from **the allergen** of claim 3; wherein the patient possesses any one of the MHC Class II DR molecules DR2, DR3, DR4 or DR7 of claim 4; wherein the patient possesses the MHC Class II molecule DR4 of claim 5; A method according

to claim 1 wherein the **polypeptide allergen is any one of Der p I, Der p II, Der fI or Der fII** and **allergens present in any of the following: grass, tree and weed (including ragweed) pollens; fungi and moulds; foods, stinging insects, the chirnomidae (non-biting midges); spiders and mites, housefly, fruit fly, sheep blow fly, screw worm fly, grain weevil, silkworm, honeybee, non-biting midge larvae, bee moth larvae, mealworm, cockroach, larvae of Tenibriomolitor beetle, mammals such as cat, dog, horse, cow, pig, sheep, rabbit, rat, guinea pig, mice and gerbil** of claim 13 for the same reasons as set forth in the Office Action mailed on 03/28/2007.

Applicant's arguments filed on 08/28/2007 have been fully considered, but are not found persuasive.

Applicants argue that

> "It is well settled law, that an applicant for patent can act as his/her own lexicographer to specifically define terms in a claim. *See, e.g., Hormone Research Foundation Inc. v. Genentech Inc.,* 904 F.2d 1558 (Fed. Cir. 1990). The specification teaches that "desensitizing a patient to a polypeptide allergen" means "inhibition or dampening of allergic tissue reactions induced by allergens in appropriately sensitized individuals" (paragraph 39 of the published application). The definition of "desensitization" does not require that the tolerance must be permanent. Thus, the references cited by the Office Action to suggest that such polypeptide allergen tolerance is not permanent does not corrupt the enablement of the instant claims. In fact, it supports the conclusion that the instant claims are enabled; those of skill in the art have been able to practice the claimed invention as claimed to achieve desensitization as defined in the instant specification.
>
> In addition, the Office Action asserts that the claims are not enabled for administering a peptide derived from the allergen. Applicants respectfully disagree. The Office Action supports its rejection by citing a number of references that allegedly show the unpredictability and adverse reactions that arise from practicing the claimed method. The conclusions drawn by the Office Action from the prior art, however, are

not in accordance with the way in which immunotherapy using peptides is considered in the art. Applicants have herewith provided copies of Francis and Larche (2005) Current Opinion in Allergy and Clinical Immunology 5, 537-43, Tarzi et al. (2006) Clinical and Experimental Allergy 36,465-74, Larche (2005) Pharmacology and Therapeutics 108, 353-61, Ali and Larche (2005) Expert Rev. Vaccines 4, 881-9, Larche (2006) Current Opinion in Immunology 18, 745-50 and Durham et al. (1999) New England Journal of Medicine 341,468-75 (Exhibits A-F). These articles show that immunotherapy using peptides is highly effective for treatment of diverse allergic diseases and that long term desensitisation is observed after such immunotherapy. In particular, Francis and Larche, the section at page 537, right hand column, bottom paragraph to page 538, left hand column, second full paragraph which discusses the fact that allergen immunotherapy has been shown to be clinically effective. The other articles support this view, which can be seen by reading the abstracts of the articles.
It is also to be noted that the articles refer at several points to the fact that unpredictable IgE mediated reactions may occur when using whole allergens and that use of peptides avoids such reactions (see for example lines 3 to 9 right hand column page 465 of Tarzi et al. and the abstract of Ali and Larche). Peptides do not cause cross-linking of IgE on mast cells and basophils, and thus adverse reactions are avoided. This is appreciated in the teaching of the present application (see page 27, lines 7 to 9 of the application), and claim 1 is directed to use of peptides, and does not cover use of whole allergens. The Office Action also cites Francis et al. to argue that desensitising patients using peptides is unpredictable. The full article has been provided with this response. As can be seen from the concluding paragraph of this article, it is acknowledged that short synthetic peptides from allergens have substantially reduced ability to cross-link IgE which means that adverse IgE mediated effects such as anaphylaxis do not occur when using such peptides. Thus, the position taken by the Office Action regarding the unpredictability associated with desensistisation is only applicable to use of whole allergens, and is not relevant to the peptides recited in claim 1.

The Examiner also refers to Kinnunen et al. to again comment on unpredictability. However, this article is written in the context of use of altered peptides, and thus the discussion of unpredictability is centered around whether T cells that recognise the natural sequence are able to cross-react with the altered ligand (see for example the conclusion in the abstract). Further Kinnunen et al. is written in the specific context of use of peptides in autoimmune disease therapy, and therefore is not directly relevant to desensitisation to an allergen.

The standard for determining enablement is whether one of skill in the art could, given the disclosure in the specification and knowledge and skill in the art, make and use the claimed invention without resorting to undue experimentation. *In re Wands,* 858 F.2d 731 (Fed. Cir. 1988). The test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt,* 537 F.2d 498 (CCPA 1976). Moreover, the fact that experimentation may even be complex

does not necessarily make it undue, if the art typically engages in such experimentation. *In re Wands.*

The Office Action asserts that the claims are not enabled, in part, because one of skill in the art would have to engage in experimentation to practice the full scope of the claimed invention. Applicants disagree. The specification teaches literally hundreds of sequences of allergens that can be used according to the instant claims. The specification further teaches how one of skill in the art can select specific peptides to use in desensitizing a patient (see, e.g., Example 6). Thus, by engaging in the type of routine experimentation, typically performed in the art and described in detail in the specification, one of skill in the art would be able to practice the full scope of the claimed invention.

In view of the foregoing, Applicants note that the art deems immunotherapy using peptides to have a long lived effect and to be predictable. Moreover, the specification and skill in the art would permit the making and using of the claimed invention without undue experimentation. Accordingly, Applicants request that the rejection be reconsidered and withdrawn."

It remains the Examiner's position that the specification does not provide sufficient enablement for the claimed method of desensitization. Applicant's argument regarding the definition of desensitization in the specification not requiring complete desensitization is persuasive. However, Applicant's characterization that Francis et al. only teaches that whole allergen immunotherapy in particular is unpredictable is not persuasive. The section of Francis et al. (PTO-892 mailed 03/28/2007, Reference W) that Applicant points to for support that immunotherapy works is actually referring to whole allergen immunotherapy, not peptide immunotherapy (In particular, the section at page 537, right hand column, bottom paragraph to page 538, left hand column, second full paragraph). Francis et al. teaches on page 538 that cat peptide vaccines are unpredictable because they can be significantly associated with adverse events, vaccination is not significant in comparison to placebo, and that of the some peptides immunotherapies that did work, they were only evident at a single time point post therapy. The

reference, written by an inventor of the instant application states "In summary, whereas such studies generally reported modest improvements in clinical and surrogate outcome measures, treatment was associated with a high frequency of adverse reactions." In addition, the co-inventor and co-author of this reference, as one of ordinary skill in the art at best, actually states in the reference that choosing peptides for immunotherapy is difficult, (not routine experimentation) (In particular, 'Further peptide vaccine design' section on page 541). The whole reference teaches though many examples that peptide selection in immunotherapy makes a difference to the outcome.

Applicant's argument that Kinnunen et al. does not apply to the claimed method because it refers to altered peptide ligands is also unpersuasive because peptides "derived" from allergens may include mutations, additions and deletions. Therefore, the claims encompass the use of altered peptide ligands for use in desensitization. Kinnunen shows that the use of altered peptide ligands in desensitization is also unpredictable.

Further, there is no example in the specification of a non-Fel d-I derived peptide, nor a plurality of non-Fel d-I derived peptides that can desensitize patients in any manner to any allergen. One of ordinary skill in the art would be required to perform a great amount of experimentation in order to identify allergens and peptides with the claimed functional characteristics to practice the claimed invention. Contrary to Applicant's assertion, it is not routine experimentation for one to determine the MHC restriction of every peptide of 5-50 amino acids of any allergen and to use those peptides to desensitize individuals.

10. Claims 1-5 and 13 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office action mailed on 03/28/2007.

Applicant is in possession of the peptides of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3 for stimulating T cells in vitro.

Applicant is not in possession of a method of desensitising a patient to a **polypeptide allergen** the method comprising administering to the patient **a peptide derived from the allergen** wherein restriction to a MHC Class II molecule possessed by the patient can be demonstrated for the peptide and **the peptide** is able to induce a late phase response in an individual who possesses the said MHC Class II molecule, wherein the **peptide has a length of 5 to 50 amino acids** and is not a Fel d I-derived peptide of claim 1; wherein **the peptide** is included in a composition containing **a plurality of peptides derived** from the **said allergen** of claim 2; wherein the **plurality of peptides derived** from said allergen includes **peptides** for which restriction to Class II DR molecules DR2, DR3, DR4 and DR7 can be demonstrated, provided that such **peptides** can be derived from **the allergen** of claim 3; wherein the patient possesses any one of the MHC Class II DR molecules DR2, DR3, DR4 or DR7 of claim 4; wherein the patient possesses the MHC Class II molecule DR4 of claim 5; A method according

to claim 1 wherein the **polypeptide allergen is any one of Der p I, Der p II, Der fI or Der fII** and **allergens present in any of the following: grass, tree and weed (including ragweed) pollens; fungi and moulds; foods, stinging insects, the chirnomidae (non-biting midges); spiders and mites, housefly, fruit fly, sheep blow fly, screw worm fly, grain weevil, silkworm, honeybee, non-biting midge larvae, bee moth larvae, mealworm, cockroach, larvae of Tenibriomolitor beetle, mammals such as cat, dog, horse, cow, pig, sheep, rabbit, rat, guinea pig, mice and gerbil** of claim 13 for the same reasons as set forth in the Office Action mailed on 03/28/2007.

Applicant's arguments filed on 08/28/2007 have been fully considered, but are not found persuasive.

Applicant argues that:

> "the specification teaches hundreds of species of polypeptide allergens and peptides thereof that can be used in according to the instant claims. Thus, the specification discloses a representative number of species of the claimed genus. Furthermore, appropriate peptides for desensitising an individual to an allergen could be obtained by routine means. As can be seen from claim 1 the peptides are required to have restriction to a MHC Class II molecule, i.e. they comprise sequence which binds to a MHC class II molecule. In order deduce the presence of such sequence within the allergen, fragments of the allergen may be tested for binding to a MHC Class II molecule, for example using the techniques described in Example 5 and 6 of the application.
>
> The invention relies on generation of a late phase response using the peptides defined in claim 1. This response is stimulated by T cells recognising peptide sequence after it has become bound to the appropriate MHC class II molecules on the surface of cells of the individual. Thus the invention is applicable to an allergen that comprises a sequence that demonstrates restriction to a MHC class II molecule. Given that a common desensitisation mechanism exists which can be used to tolerise against an allergen that contains sequence which demonstrates restriction to a MHC class II molecule, then no

> further description is needed of the peptide sequences for the skilled person to carry out the invention, and there is adequate written description in the application as filed."

It is the Examiner's position that the specification has not adequately described a correlation between function (desensitization) and structure responsible for desensitization such that one of ordinary skill in the art would have known what peptides encompassed by claims could be generated to have the disclosed function of desensitization. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features See University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895. "Without a correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement." Ex parte Kubin, 83 U.S.P.Q.2d 1410 (BPAI 2007). The specification does not adequately describe the genus of peptides derived from any non-Fel d I allergen for use in the claimed method for desensitization.

11. The following new grounds of rejection are necessitated by the amendment filed on 08/28/2007.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-5 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/24281 (IDS filed on 04/24/2007, Reference BE).

WO 94/24281 teaches a method of desensitising a patient to a Der p I or Der p II dust mite polypeptide allergen the method comprising administering to the patient one or more peptides derived from the allergen, wherein the peptide has a length of 5 to 50 amino acids and is not a Fel d I-derived peptide (In particular, abstract, whole document).

The limitations of "wherein restriction to a MHC Class II molecule possessed by the patient can be demonstrated for the peptide" and "the peptide is able to induce a late phase response in an individual who possesses the said MHC Class II molecule" of claim 1; "wherein the plurality of peptides derived from said allergen includes peptides for which restriction to Class II DR molecules DR2, DR3, DR4 and DR7 can be demonstrated, provided that such peptides can be derived from the allergen" of claim 3; "wherein the patient possesses any one of the MHC Class II DR molecules DR2, DR3, DR4 or DR7" of claim 4; "wherein the patient possesses the MHC Class II molecule DR4" of claim 5 are inherent as the same peptide is being administered to the same patient population for the same result. Since the office does not have a laboratory to test the reference peptides, it is applicant's burden to show that the reference peptides are not the peptides recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA

1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

14. Claims 1, 4-5 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Higgins et al. (IDS filed on 09/22/2004, Reference 28).

Hoyne teaches a method of desensitising a patient to a Der p I polypeptide allergen the method comprising administering to the patient a peptides derived from the allergen, wherein the peptide has a length of 29 amino acids and is not a Fel d I-derived peptide (In particular, abstract, whole document).

The limitations of "wherein restriction to a MHC Class II molecule possessed by the patient can be demonstrated for the peptide" and "the peptide is able to induce a late phase response in an individual who possesses the said MHC Class II molecule" of claim 1; "wherein the plurality of peptides derived from said allergen includes peptides for which restriction to Class II DR molecules DR2, DR3, DR4 and DR7 can be demonstrated, provided that such peptides can be derived from the allergen" of claim 3; "wherein the patient possesses any one of the MHC Class II DR molecules DR2, DR3, DR4 or DR7" of claim 4; "wherein the patient possesses the MHC Class II molecule DR4" of claim 5 are inherent as the same peptide is being

administered to the same patient population for the same result. Since the office does not have a laboratory to test the reference peptides, it is applicant's burden to show that the reference peptides are not the peptides recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 12, 2007

Nora M. Rooney, M.S., J.D.

Patent Examiner

Technology Center 1600

Maher Haddad

MAHER M. HADDAD
PRIMARY EXAMINER